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## (54) IMPROVEMENTS IN OR RELATING TO 1-HYDROXY-3-OXO-BENZIMIDAZOLES, QUINOXALINE-DI-N-OXIDES AND BENZIMIDAZOLE-MONO- AND DI-N-OXIDES

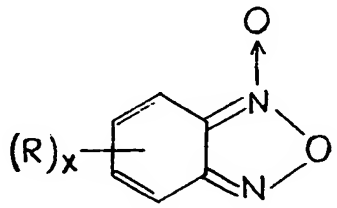
(71) We, RESEARCH CORPORATION, of 405 Lexington Avenue, New York, New York, 10017, United States of America, a Corporation organised under the laws of the State of New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

This invention relates to quinoxaline-di-N-oxides, and benzimidazole-mono and di-N-oxides. The compounds of the present invention are useful in the control of various pathogenic microorganisms. As shown in U.S. Patent No. 3,047,579, such compounds are generally prepared by processes involving the direct oxidation of quinoxaline compounds and usually require a corresponding quinoxaline compound as the starting material. Oxidation reactions are generally known to be somewhat non-selective and may give rise to low yields of the desired product together with one or more by-products which can be difficult to separate.

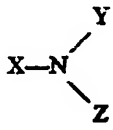
Our British Patent No. 1,215,815 discloses and claims a process for producing quinoxaline-di-N-oxides and benzimidazole mono- and di-N-oxides which comprises reacting a compound containing a methylene group which is activated by two electron withdrawing-groups, or a compound containing a methylene group which is activated by one electron-withdrawing group, said one electron-withdrawing group being a nitro group or a carbonyl group of a ketone or an aldehyde, with an isobenzofuroxan in the presence of a base.

Processes for producing quinoxaline di-N-oxides which comprise the following step (which is claimed in British Patent No. 1,187,991) are, however, specifically disclaimed from Patent No. 1,215,815, namely the step of reacting a compound which contains a ketonic or aldehydic carbonyl group and which has a methylene group in a position

adjacent the carbonyl group with at least equimolar quantities of both a benzofuroxane N-oxide of the following general formula:—



in which
x represents 1 or 2;
R represents a hydrogen or halogen atom, or an alkyl, alkoxy, carbalkoxy or carbaryloxy group or the radical



in which
X denotes —$SO_2$— or —CO—;
Y denotes a hydrogen atom or an alkyl radical; and
Z denotes (1) a hydrogen atom; (2) an alkyl radical; (3) a cycloalkyl radical having 5 to 8 carbon atoms in the ring system; (4) an aryl radical which may be substituted from one to three times by alkyl or alkoxy radical containing 1 to 6 carbon atoms, or a halogen atom; or (5) a heterocyclic radical; or Y and Z together with the nitrogen atom which links them form a heterocyclic radical;
or two radicals R together form a fused benzene ring, and of a primary aliphatic or cycloaliphatic amine or ammonia, or with at least an equimolar quantity of a corresponding Schiff's base, which process is carried out in an organic diluent at a temperature of from 20 to 100°C.

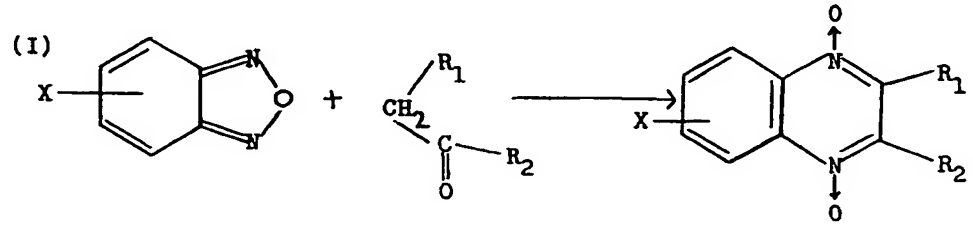
The present invention is an improvement in or modification of the method of our British Patent No. 1,215,815. We have found that, in accordance with the present invention, quinoxaline di-N-oxides, 1-hydroxy-3-oxo-benzimidazoles or benzimidazole-di-N-oxides can be prepared by reacting an isobenzofuroxan with a malonamate, a malonic acid diamide, malononitrile, a heterocyclic ketone, a pyruvaldehyde acetal other than the dimethyl acetal (the use of which is claimed in Specification No. 1,215,815) a lower alkoxy $\gamma,\gamma$-di(lower-alkoxy) aceto acetate other than ethyl $\gamma,\gamma$-diethoxy aceto acetate (the use of which is claimed in Specification No. 1,215,815), a $\beta$-keto ester, a $\beta$-diketone, a $\beta$-keto amide, a primary or secondary nitro compound, a malonic acid diester, cyano acetamide an alicyclic ketone, a keto sulfonyl compound or a ketosulfonamide in the presence of a base.

In the method of the present invention, certain specific bases are used with certain reactants. Thus when the reactant is a malonic acid diester the base is either an alkali metal hydroxide or an alkali metal hydride. When the reactant is a malonamate, or an alicyclic ketone, the base is an alkali metal hydroxide, an alkali metal hydride or an alkali metal alkoxide. With a $\beta$-keto ester or a $\beta$-diketone, the base is ammonia, a primary or a secondary amine or an alkali metal hydride. With $\beta$-keto amides the base is a tertiary amine or an alkali metal hydroxide, hydride or alkoxide. With a heterocyclic ketone, the base is ammonia, a primary, secondary or tertiary amine, or an alkali metal hydroxide, alkoxide or hydride. When the reactant is either malonitrile, or cyano acetamide, the base is an alkali metal hydride. When the reactant is a pyruvaldehyde acetal, the base is ammonia, a primary, secondary or tertiary amine. When the reactant is a lower alkyl $\gamma,\gamma$-di- (lower alkoxy) acetoacetate, the base is ammonia, a primary, secondary or tertiary amine, an alkali metal hydroxide, hydride or alkoxide. When the reactant is a primary or secondary nitro compound the base is an alkali metal hydroxide, an alkali metal alkoxide or an alkali metal hydride.

In the case of $\beta$-keto esters and malonic acid diesters, when an alkali metal alkoxide is used, it is preferable to use an alkoxide having the same alkyl group as the reactant to avoid ester interchange.

The preparative reactions of the present invention may be exemplified by the following general reaction:—

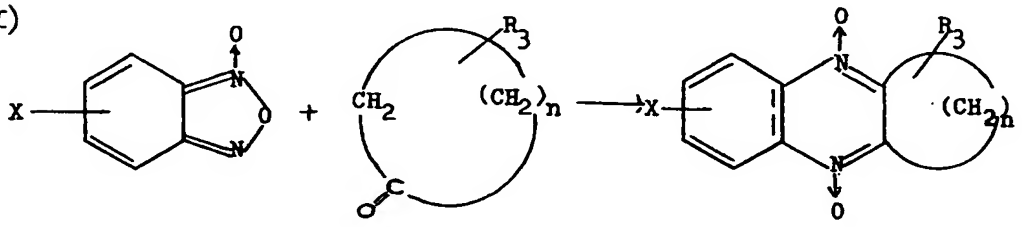
(I)



In this sequence, the compound $R_1CH_2 \cdot CO \cdot R_2$ is a malonamate, a malonic acid diamide; malonitrile, a heterocyclic ketone, a pyruvaldehyde acetal, a β-keto ester, a β-diketone, a lower alkyl γ,γ-di(lower alkoxy) aceto acetate, a β-keto amide, a malonic acid diester, a cyano acetamide, an alicyclic ketone, a keto-sulphonyl compound, or a ketosulphonamide.

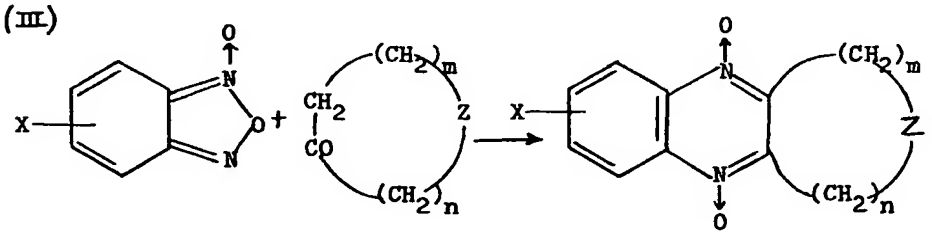
Reaction sequence (I) is more specifically illustrated in the following reaction sequences is (II) to (IIIE):—

(II)



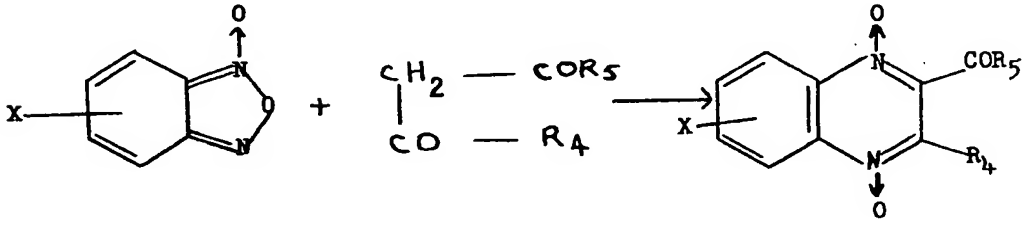
Here, $R_1$ and $R_2$ of sequence (I) are taken together to form an alicyclic ring in which n = 2 to 16. The alicyclic ring may be substituted with a substituent $R_3$ such as halogen, hydroxyl, alkoxyl, acetoxyl, alkyl, aryl, acetal, amino, substituted amino, e.g. alkylamino, arylamino, acylamino, aroylamino, and electron withdrawing groups such as carboxy, carbalkoxy, nitrile and amide.

(III)



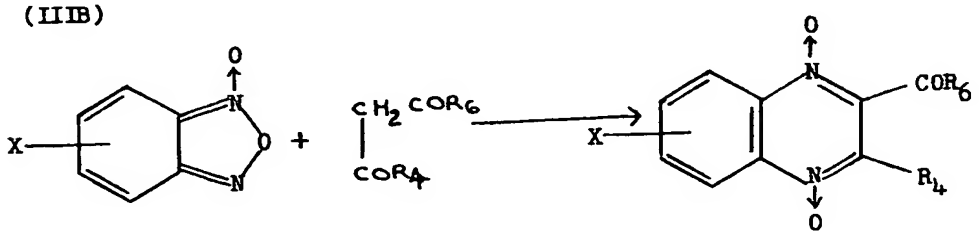
Here, the carbonyl group and the adjacent methylene group of reactant (b) in sequence I form part of a heterocyclic ring, e.g. a heterocyclic ketone, where m = 0 or 1 and n = 2 or 3. The hetero atom Z can be oxygen, sulfur, imino (NH) or substituted imino, wherein the substituent on the nitrogen may, for example, be alkyl, aryl, such as phenyl, acyl, such as acetyl, or aroyl. As in sequence II, the ring may be substituted by substituent $R_3$. When m = (n−1), two isomeric products will be formed.

(IIIA)



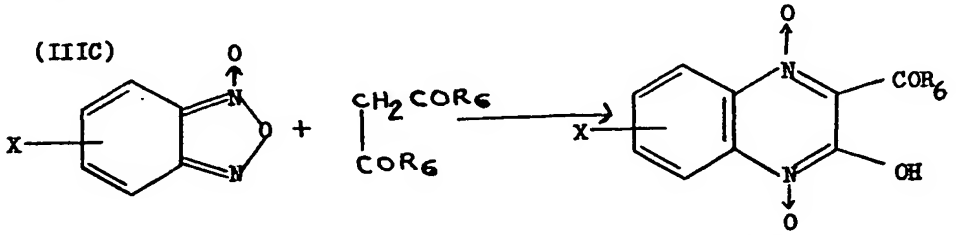
Here, $R_4$ or $R_5$ may be hydrogen and either or both may be alkyl groups, e.g., of 1 to 6 carbon atoms, substituted alkyl groups or aryl groups. Appropriate substituents for $R_4$ and $R_5$ are as exemplified in reaction II under the definition of $R_3$.

(IIIB)



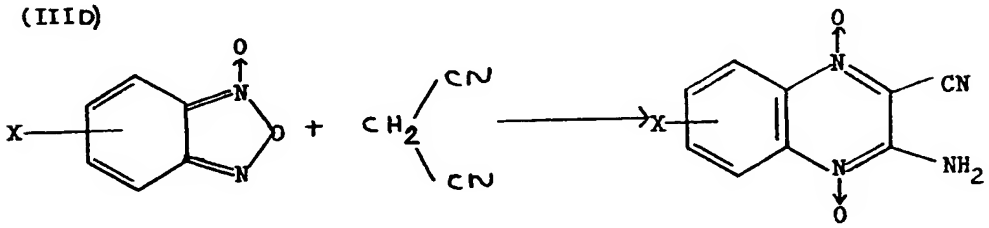
Here, $R_4$ is as exemplified as in (IIIA) and $R_6$ may be $OR_7$, where $R_7$ is alkyl, aryl or alkaryl; or $NR_8R_9$ where $R_8$ and $R_9$ may be hydrogen, alkyl or aryl, e.g., phenyl.

(IIIC)

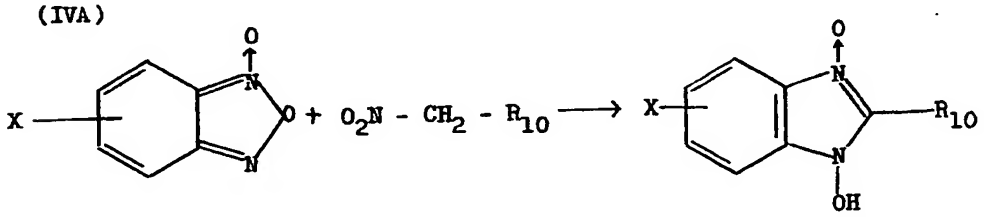


Here, $R_6$, for example, is $OR_7$ or $NR_8R_9$, in which $R_7$, $R_8$ and $R_9$ are as exemplified in (IIIB). The product of this reaction sequence may include the reduced form of the indicated di-N-oxide.

(IIID)

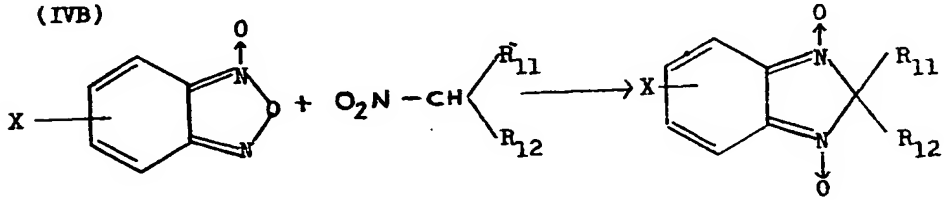


(IVA)



In this sequence $R_{10}$ is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, carbalkoxy, or carboxamido,

(IVB)



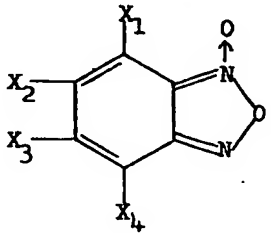
In this sequence $R_{11}$ and $R_{12}$ are as exemplified as $R_{1a}$ in (IVa) with the exception of hydrogen, or taken together form a carbocyclic ring or substituted carbocyclic ring, with substituents as previously described.

Reaction sequences I to IIID above concern the reaction between a benzofuroxan with a methylene-containing compound activated by one or two electron-withdrawing groups to provide a quinoxaline-di-N-oxide. Reaction sequences IVA and IVB above deal with the reaction between a benzofuroxan with primary and secondary nitro compounds. As is evident, the primary nitro compounds yield hydroxy benzimidazole-N-oxides (IVA) whereas the secondary derivatives provide the benzimidazole-di-N-oxides (IVB).

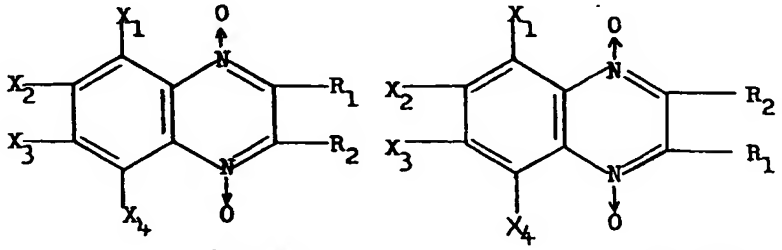
Although only one substituent X is illustrated in each of the above sequences and in most of the following formulae there may be up to four substituents on the fused aryl moiety of the benzofuroxan, each of which may be different.

For example, one or more of the following substituents can be present: hydrogen, lower alkyl, lower alkoxy, chloro, bromo, fluoro, trifluoromethyl, di(lower alkyl)amino, amino, carboxy, carbamyl, carbo(lower alkoxy), lower alkylmercapto, lower alkylsulfoxy, lower alkylsulfonyl, sulfonamideo, N-(lower alkyl)sulfonamido and N,N-di(lower alkyl)sulfonamido. (In this Specification the terms "lower alkyl", "lower alkanoyl", and "lower alkoxy" respectively mean an alkyl, alkanoyl and alkoxy group having seven or fewer carbon atoms). The favored positions on the aryl ring of the benzofuroxan are the 5- and/or 6-positions. Of special interest for these positions are at least one of the following substituents: hydrogen, methyl, chloro, fluoro, trifluoromethyl, methoxy and sulfonamido. Where both singly or multiply-substituted compounds can be be used, a singly-substituted compound, that is, a 5- or 6-substituted compound would be preferred to a 5,6-disubstituted derivative for reasons of economy in manufacture as regards the benzofuroxan reactant. Nitro, hydroxy and mercapto groups are not desirable substituents since they retard the reaction and/or give undesired products and/or poor yields.

The locations of the substituents $X_1$, $X_2$, $X_3$, and $X_4$ illustrated herein is somewhat arbitrary since the exact points of attachment of the methylene-containing compound to the benzofuran are difficult to predict. For example, if a benzofuroxan of the formula



is reacted with a reactant $R_1—CH_2—COR_2$, two products are possible as shown by the formulae below:—



(III-A) (III-B)

In formula III—A, the groups $X_1$, $X_2$, $X_3$ and $X_4$ are attached to the 5, 6, 7 and 8-positions whereas in III—B, they are attached to the 8, 7, 6, 5-positions of the quinoxaline-di-N-oxide product. The examples herein use the first system of nomenclature. It must be remembered throughout that this designation is purely arbitrary except in the case where $X_1 = X_4$ and $X_2 = X_3$, and in the case wherein all four substituents are alike.

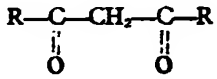
Benzofuroxan or a substituted benzofuroxan can be used in the process of this invention. Such benzofuroxans are readily available or easily prepared by those skilled

in the art. For instance, the preparation of various substituted benzofuroxans is described by Kaufman et al. in Chem. Rev. 59, 448 (1959) in an article entitled "The Furoxans".

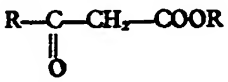
As previously stated, the reactants which may be used in accordance with the present invention are malonamates, β-ketoesters, β-diketones, malonic acid diesters, malononitriles, malonic acid diamides, heterocyclic ketones, alicyclic ketones, β-ketoamides, ester-amides, ketosulfonyl compounds, ketosulfonamides, pyruvaldehyde, acetals and primary and secondary nitro compounds.

The preferred β-diketones, β-ketoesters and malonic esters which may be used in accordance with the present invention have the following general formulae, respectively:

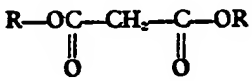
(VII)



(VIII)



(IX)

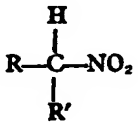


wherein the R groups represent alkyl groups containing from 1 to 4 carbon atoms which may be alike or different.

In the preparation of quinoxaline-di-N-oxides, particularly with the malonate reactants, a proportion of the corresponding quinoxaline compound is formed along with the quinoxaline-di-N-oxide. The compound of reduced form may be separated by conventional separation techniques, e.g., filtration of the reaction mixture, followed by recovery of the quinoxaline-di-N-oxide from the filtrate. With malonamates, that is, half-ester, half-amide derivatives of malonic acid, the quinoxaline compound appears to be the predominant product.

Reaction sequences IVA and B above illustrate the reaction between a benzofuran with a nitro compound. If the nitro compound is of the primary type, that is, where there is a $CH_2$ group alpha to the nitro group, then the resulting product is a 1-hydroxy-3-oxide illustrated by reaction IVA. Alternatively, if the nitro compound is of the secondary type, that is where the adjacent carbon atom has only one hydrogen attached, the resulting product is a benzimidazole-1,3-di-N-oxide. Although the mechanism involved in reaction sequences I to (IIID) and (IVA) (IVB) are similar, in the latter there is a marked difference in the type of products obtained. As is evident, the quinoxaline-di-N-oxides contain a six membered B ring whereas the benzimidazoles contain a five-membered B ring. With regard to the organo nitro reactant, compounds encompassed by the following general structure are preferred for the process of this invention:

(X)



wherein R is alkyl having 1 to 4 carbon atoms, and R′ is H or alkyl having 1 to 4 carbon atoms.

The reaction sequences described above (I to IVB) must be effected in the presence of a base. A variety of bases may be used, for example organic amines, ammonia, alkali metal hydroxides, hydrides and alkoxides.

Representative of such bases are ammonia, primary amines such as n-propylamine, n-butylamine, aniline, cyclohexylamine, benzylamine, p-toluidine, ethylamine, n-octylamine; secondary amines such as di-ethylamine, di-n-propylamine, methyl-n-butylamine, pyrrolidine, morpholine, piperidine, pyrrole, pyrroline, N-methylaniline, N-methylbenzylamine, pyrimidine; tertiary amines such as triethylamine, trimethylamine, N,N-dimethylaniline, N-methylpyrrolidine, N,N-dimethylpyrimidine, N-methylmorpholine, and 1,5-diazabicyclo-5-nonene; sodium hydroxide, potassium hydroxide, ammonium hydroxide, sodium ethoxide, potassium methoxide, and sodium hydride.

The amount of base used in any of the reactions discussed herein is not critical but can vary widely, e.g. from a trace or catalytic amount of base, that is, from about 0.001 percent by weight based on the benzofuroxan reactant present, to even molar excess amounts, as occurs when the base is used as solvent. In general, optimum amounts range from about 0.1 percent by weight to about equimolar amounts based on the benzofuran used. As will be readily appreciated, the optimum proportion of base will vary with the nature of the particular reactants employed, as well as specific reaction conditions. Accordingly, the optimum proportion of base is most conveniently established by routine experimentation using small scale laboratory reactions.

The inclusion of a solvent in the basic process of this invention is not critical and its desirability will depend on many factors e.g. the consistency of the reaction mixture, the temperature desired, the ease of maintaining a given temperature.

If the reactants when combined produce a viscous system or if temperature control is difficult, it is highly desirable to include an appropriate solvent. For purposes of this invention, an appropriate solvent is any solvent which does not react in an undesired way with either the reactants or the final products.

By choosing an appropriate solvent, better temperature control is possible since specific elevated reaction temperatures can be attained by selecting a solvent having the desired boiling point. Suitable solvents are aromatic hydrocarbons such as benzene, toluene, xylene; acetonitrile, N,N-dimethylformamide, halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, alcohols such as methanol, ethanol, propanol, n-butanol, ethers such as diethyl ether, dioxane, tetrahydrofuran, ethylene glycol and ethers of ethylene and diethylene glycol. Additionally, an excess of the base can be used as solvent provided, of course, it is liquid at the reaction temperature employed. This provision, as those skilled in the art will recognize, limits the use of bases as solvents to organic amines. In such instances, the base is present in great excess relative to the benzofuroxan reactant.

Reaction temperatures do not appear to be critical in the present process although it is generally preferred to carry out the reaction at temperatures above room temperature. A preferred range is from about 30°C to about 100°C. Temperatures below 30°C may be employed for instance 0°C to 30°C but are less preferred because of the relative slowness of the reaction and generally poorer yields.

The time required for the reaction will vary considerably with the nature of the reactants, the base used, and the temperature. Reaction periods ranging from about 15 minutes to about 30 hours give substantial yields of the desired products. Higher temperatures, as expected, require shorter reaction periods than do lower temperatures for a given set of reactants. In general, reaction periods of from about 15 minutes to about 12 hours are adequate.

The molar ratio of reactants, that is, of the benzofuroxan and the methylene-activated reactant, is not critical but can vary widely, e.g. from equimolar proportions to a large excess of either reactant. They are, in general, reacted in equimolar proportions. As a practical measure when using a readily available methylene-activated reactant e.g. acetone, a large excess of the reactant is used to ensure as complete a conversion of the benzofuroxan to the desired product as is possible. Further, the excess methylene-activated reactant can also serve as solvent.

The order of addition of reactants is not critical to the success of the process. They can be added all at once along with the base or the base can be added to a mixture of the benzofuroxan and methylene-activated reactant. This latter method is advantageous in the case of exothermic reactions since it facilitates temperature control apparently by regulating the rate of reaction. In the case of such exothermic reactions, the use of an appropriate solvent also contributes to temperature control. As alternatives to the above method of addition of reactants, either reactant can be added to the other in the presence of the proper base, or the reactants can be added simultaneously to the base.

When benzofuroxan reacts with a symmetrical $\beta$-diketone (formula VII) there is no question as to the structure of the product involved since the steric effects of the R groups are identical. However, when unsymmetrical $\beta$-diketones (formula VII R groups are not alike) react with benzofuroxan, a single product or isomeric products are possible, depending upon the steric effects of the R groups. A series of reactions with 1-benzoyl-2-alkanones ($C_6H_5$—CO—$CH_2$—CO—R wherein R is methyl, ethyl, i-propyl or t-butyl; as the methylene-activated reactants clearly demonstrate the steric effects of the R group. When reacted with benzofuroxan in the presence of triethylamine or diethylamine as base, the first two members of the series produced only 2—R—3 benzoylquinoxaline-di-N-oxide (R = methyl, ethyl). The third member produced an isomeric mixture of 2-isopropyl-3-benzoylquinoxaline-di-N-oxide and 2-isobutyryl-3-

phenylquinoxaline-di-N-oxide. The fourth member gave 2-pivalyl-3-phenylquinoxaline-di-N-oxide as the only product isolated.

A second series of reactions using p-(substituted) benzoyl acetones as the methylene-activated reactant produced a single product-2-methyl-3-p-(substituted)benzoylquinoxaline-di-N-oxide-regardless of the nature of the p-substituent.

With regard to the isolation of the desired products of this invention, it is found in many instances that in the course of or upon completion of reaction the product precipitates out in crystalline form. In such cases, all that is required is filtration, washing and drying. If, on the other hand, the product does not completely precipitate or if it remains in solution, the reaction workup consists of evaporating the mixture almost to dryness and then filtering the product. If the sodium salt of the product forms as it does in certain instances, the general procedure consists of filtering said salt, dissolving it in water, acidifying the solution and subsequently filtering the product which forms. All of the above techniques are well known to those skilled in the art.

Chemical and physical evidence confirm the di-N-oxide structure of products obtained from reaction scheme I. For example, the infrared spectrum of the product of the reaction of dibenzoylmethane and benzofuroxan, assigned the structure 2-phenyl-3-benzoylquinoxaline-di-N-oxide, displayed strong bands at 1670 $cm^{-1}$ (conjugated carbonyl), 1335 (N-oxide), 770 (ortho-substituted phenyl) and 690 (monosubstituted phenyl). Reduction with sodium dithionite gave a product identical (mixed melting point and infrared spectrum) with a sample of 2-phenyl-3-benzoylquinoxaline prepared according to the method of Brandt et al. Ann. 688, 189 (1965).

The product from benzofuroxan and acetylacetone was assigned the structure 2-methyl-3-acetylquinoxaline-di-N-oxide. Its nmr spectrum showed singlets at 7.55 (3H) and 7.34 (3H) and two multiplets centered at 2.24 (3H) and 1.52 (3H) respectively, and its infrared spectrum showed intense bands at 1700 $cm^{-1}$ (carbonyl) 1330 (N-oxide) and 770 (ortho-substituted phenyl). These data are consistent with the assigned structure.

The verification that the herein disclosed compounds are effective antimicrobial agents is established by experimental evaluations. One such *in vivo* evaluation consists of seeding nutrient broth containing various concentrations of the subject compounds with a particular organism and subsequently determining the "minimum inhibitory concentration" (MIC). The MIC is defined as the minimum concentration of the antimicrobial test compound (in micrograms/milliliter) at which growth of the microorganism failed to occur. For instance, the following are representative of the compounds disclosed herein which have exhibited *in vitro* activity in the above described procedure:—

2,3-trimethylenequinoxaline-di-N-oxide 1-hydroxybenzimidazole-3-oxide

Since all the products of the present invention possess *in vitro* activity against harmful microorganisms, they are useful as industrial antimicrobials, for instance, water-treatment, slime-control, paint preservation, wood preservation, and so forth, as well as for topical application purposes, for example, disinfectants, and so forth. In the latter application, it will often be convenient to compound the selected product with a pharmaceutically acceptable carrier for ease in application. Thus, for example, they may be blended with vegetable or mineral oils or incorporated in emollient creams. Similarly, they may be dissolved or dispersed in liquid carriers or solvents such as water, alcohol, glycols or mixtures thereof or other reaction-inert media, that is media which have no harmful effect on the active ingredient. For such purposes, it will generally be acceptable to employ concentrations of active ingredients of from about 0.01 percent to about 10 percent by weight based on total composition.

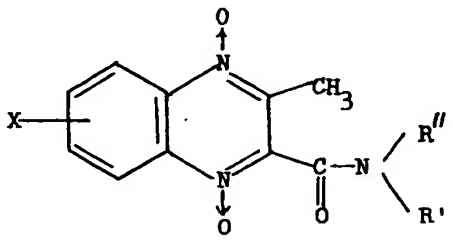
Furthermore, many of the compounds described herein find particular utility in the growth promotion of animals in the control of chronic respiratory disease in poultry, infectious sinusitis in turkeys, and urinary tract and systemic and non-systemic infections in animals, including man.

Additionally, many of the novel compounds described herein are effective against gram-positive and/or gram-negative bacteria *in vivo*. This broad spectrum activity, that is, activity against both gram-positive and gram-negative bacteria, is in contrast to the typical gram-negative activity exhibited by quinoxaline-di-N-oxides in general.

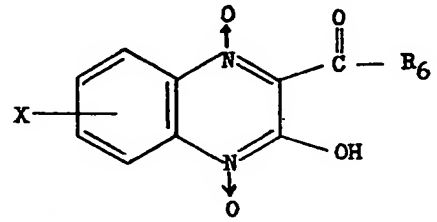
As will be obvious to those skilled in the art, many of the products described herein are valuable intermediates for the production of more highly substituted quinoxaline-di-N-oxides. For example, the products bearing a methyl substituent, e.g. 3-methyl-2-quinoxalinecarboxamide-di-N-oxide, can be brominated to the corresponding bromomethyl derivative, which can then be converted by known methods to an ether, a thio-

ether, an amine or substituted amine, a mercapto or hydroxy group. Still further, products bearing an hydroxy or mercapto group can be converted to acyloxy, acylthio, ether or thioethers.

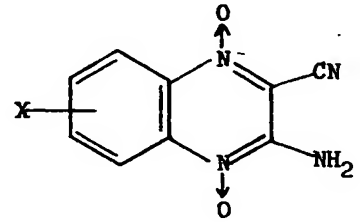
The present invention also includes the novel compounds of the following general formulae which can be prepared by a method in accordance with the method of British Patent No. 1,215,815:—



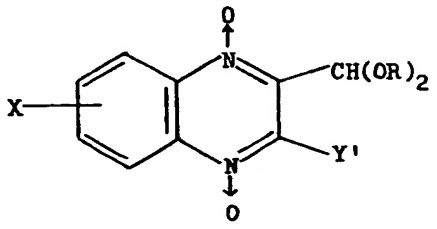
wherein X is fluoro, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different, and each of R′ and R″ is hydrogen or lower alkyl.



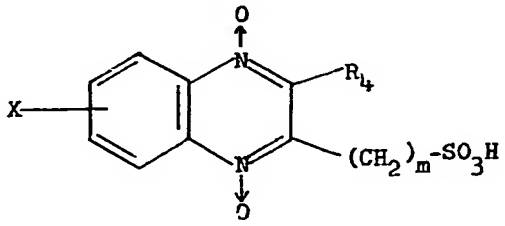
wherein $R_6$ is lower alkoxy, aryloxy, benzyloxy or $NR_8R_9$ wherein $R_8$ and $R_9$ are hydrogen, lower alkyl or phenyl; and X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido, and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different, the compound 2-carbomethoxy-3-hydroxy-quinoline di-N-oxide and 2-carboethoxy-3-hydroxy-quinoline di-N-oxide, which are claimed in Specification No. 1,215,815, being excluded.



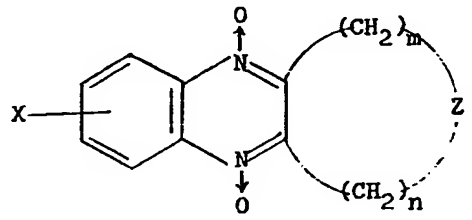
wherein X is fluoro trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido, and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different.



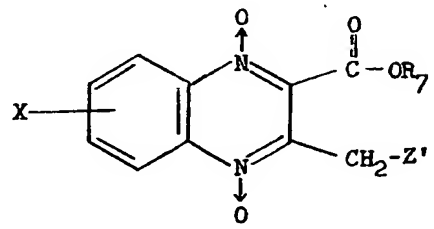
wherein R is lower alkyl; X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido, or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different, and Y' is hydrogen, or carbo (lower alkoxy), the compounds 2-formyl-dimethyl-acetal-quinoxaline di-N-oxide and 2-carboethoxy 3-formyl-di-ethyl-acetal-quinoxaline di-N-oxide, which are claimed in Specification No. 1,215,815, being excluded.



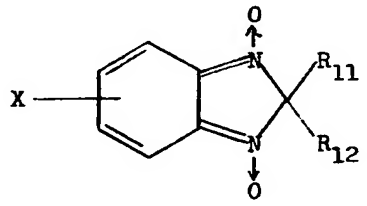
wherein X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; $R_4$ is lower alkyl or phenyl; and m is 0 or 1.



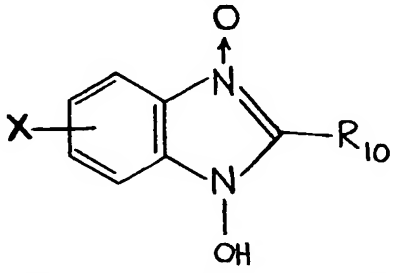
wherein X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; Z is oxygen, sulfur, imino or N-methylimino; m is 0 or 1 and n is 2 or 3.



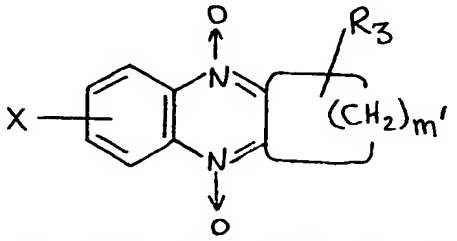
wherein X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; $R_7$ is lower alkyl; and Z' is halogen, lower alkoxy, lower alkanoyloxy, cyano, amino, phenoxy, mercapto or lower alkylmercapto.



wherein X is fluoro, chloro, methoxy, sulfonamido, hydrogen, methyl, N-methylsulfonamido, N,N-dimethyl sulfonamido or trifluoromethyl and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; $R_{11}$ and $R_{12}$ are methyl, ethyl, a methyl or ethyl group substituted by a chloro, bromo, hydroxy or diethylamino radical or, when taken together with the carbon atom to which they are attached, are cyclohexyl, the compounds 2,2-dimethyl-2H benzimidazole-1,3 dioxide and 2-methyl, 2-ethyl-2H-benzimidazole 1,3 dioxide, which are claimed in Specification No. 1,215,815, being excluded.



wherein X is hydrogen, fluoro, chloro, methoxy, methyl, trifluoromethyl, sulphonamido N-methylsulphonamido or N,N-dimethyl-sulphonamido, and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; $R_{10}$ is hydrogen, alkyl, aryl, carbalkoxy, carboxamido, substituted alkyl or substituted aryl, the compounds 1-hydroxy-2-benzimidazole-proprionamide-3-oxide and 1-hydroxy-2-carboethoxybenzimidazole-3-oxide, which are claimed in Specification No. 1,215,815, being excluded.



wherein X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethyl-sulfonamido, and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different, m' is an integer from 2 to 16, and $R_3$ is halogen, hydroxyl, alkoxy, acetoxy, alkyl, aryl, acetyl, amino, alkylamino, arylamino, acylamino, aroylamino, carboxy, carbalkoxy, nitrile or amide.

The following examples illustrate the compounds of the present invention, which may be prepared by the methods of this invention or by the method of British Patent No. 1,215,815.

## EXAMPLE I.

### 2-Methyl-3-Acetylquinoxaline-di-N-oxide

To a stirred mixture of benzofuroxan (6.8 g., 0.05 mole) and acetyl acetone (5.0 g., 0.05 mole) in 40 mL tetrahydrofuran is added n-propylamine (2.96 g., 0.05 mole). The reaction mixture is stirred overnight at room temperature and then evaporated under reduced pressure to a slurry. This residue is triturated with ether and filtered to recover 0.9 g of yellow solid which, upon crystallization from chloroform-n-hexane, is reduced to 0.33 g. of the title compound melting at 146—149°C. (MIC against Vibrio comma is 3.12 meg/ml.). Further purification is achieved by recrystallization from methanol.

The n.m.r. spectrum of the product showed singlets $\tau$ 7.55 (3H) and $\tau$ 7.34 (3H), and multiplets centered at $\tau$ 2.24 (2H) and $\tau$ 1.52 (2H) in deuterated chloroform with TMS as internal reference set at 10 (Varian A—60 spectrometer).

Infrared: 1700, 1510, 1330, 1270, 1100, 1050, 830, 770 $cm^{-1}$

Analysis: Calc'd for $C_{11}H_{10}O_3N_2$: %C, 60.54; %H, 4.62; %N, 12.84

Found: %C, 60.48; %H, 4.70; %N, 12.33

## EXAMPLE II.

2-Methyl-3-Carboethoxyquinoxaline-di-N-Oxide

To a solution of benzofuroxan (6.8 g., 0.05 mole) and ethyl-acetoacetate (6.51 g., 0.05 mole) in 40 ml. tetrahydrofuran is added n-propylamine (2.96 g., 0.05 mole). The reaction mixture is stirred for 36 hours and filtered to separate a trace of tan solid. The filtrate is evaporated at reduced pressure to a slurry and triturated with chloroform-hexane. After refrigeration storage, the slurry is filtered to recover 4.29 g. of product in the form of a tan solid which is purified by recrystallization from chloroform-hexane with activated carbon treatment.

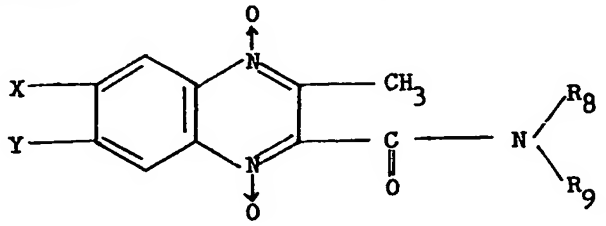
Infrared: 1730, 1510, 1330, 1275, 1340, 1050, 1010, 1000, 770 $cm^{-1}$

Analysis: Calc'd for $C_{12}H_{12}N_2O_5$: %C, 58.06; %H, 4.87; %N, 11.29

Found: %C, 58.27; %H, 4.74; %N, 10.98

## EXAMPLE III.

In each of the following cases equimolar (0.1 m) quantities of benzofuroxan and the appropriate N-substituted acetoacetamide are allowed to stand with 10 ml of diethylamine and 100 ml tetrahydrofuran for two hours. The material which precipates is filtered, dried and recrystallised from a chloroform-methanol (1:1) mixture. The following compounds result



wherein:—

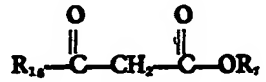
| X | Y | $R_8$ | $R_9$ | M.P. (°C) |
|---|---|---|---|---|
| H | H | $CH_3$ | H | 223 |
| H | H | $C_2H_5$ | H | 213– 4 |
| H | H | n-$C_3H_7$ | H | 175 |
| H | H | $CH_3$ | $CH_3$ | 193– 4 |
| H | H | $C_2H_5$ | $C_2H_5$ | 162– 4 |
| H | H | i-$C_3H_7$ | H | 217– 8 |
| H | H | n-$C_4H_9$ | H | 148 |
| H | H | $C_7H_7$ | H | 218– 9 |
| Cl | H | $CH_3$ | H | 220– 1 |
| $OCH_3$ | H | $CH_3$ | H | 236– 7 |
| Br | H | $C_2H_5$ | H | 207 |
| F | H | $C_2H_5$ | H | 222– 3 |
| Cl | H | $CH_3$ | $CH_3$ | 194– 5 |
| Cl | H | $C_2H_5$ | $C_2H_5$ | 169– 70 |
| $OCH_3$ | H | H | H | 262 |
| $CF_3$ | H | H | H | 230 |
| F | H | H | H | 243– 4 |

TABLE (Continued)

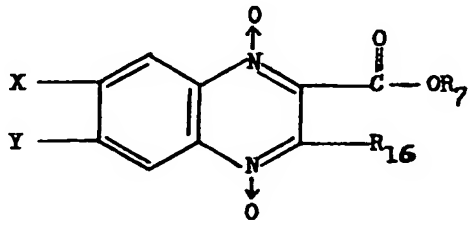
| X | Y | $R_8$ | $R_9$ | M.P. (°C) |
|---|---|---|---|---|
| F | H | $CH_3$ | H | 232– 3 |
| Br | H | H | H | 237 |
| Cl | H | H | H | 237 |
| $CH_3$ | H | H | H | 246 |
| $CH_3$ | $CH_3$ | H | H | 263– 4 |
| Cl | Cl | H | H | 251 |
| $OCH_3$ | H | H | $C_2H_5$ | 233 |
| Br | H | $CH_3$ | H | 223 |
| Cl | Cl | H | $CH_3$ | 225 |
| Cl | H | H | $C_2H_5$ | 216– 8 |
| Cl | Cl | H | $C_2H_5$ | 220 |
| Cl | H | H | n-$C_3H_7$ | 208 |
| Cl | H | H | i-$C_3H_7$ | 216– 7 |
| H | H | H | i-$C_4H_9$ | 156– 7 |
| H | H | H | sec-$C_4H_9$ | 199–200 |
| H | H | H | allyl | 154 |
| Cl | H | H | allyl | 165 |
| H | H | $-CH_2CH_2CH_2CH_2-$ | | 188– 9 |
| Cl | H | $-CH_2CH_2CH_2CH_2-$ | | 214– 5 |
| H | H | $-CH_2CH_2CH_2CH_2CH_2-$ | | 174– 6 |
| Cl | H | $-CH_2CH_2CH_2CH_2CH_2-$ | | 218 |
| H | $SO_2NH_2$ | H | H | 230– 2 |
| H | $SO_2NH_2$ | $CH_3$ | H | 216– 7 |
| H | $SO_2NH_2$ | $CH_3$ | $CH_3$ | 220– 2 |
| H | $SO_2NH(CH_3)$ | H | H | 215– 7 |
| H | $SO_2NH(CH_3)$ | $CH_3$ | H | 209– 10 |
| H | $SO_2NH(CH_3)$ | $CH_3$ | $CH_3$ | 227– 9 |
| H | $SO_2N(CH_3)_2$ | H | H | 232– 3 |
| H | $SO_2N(CH_3)_2$ | $CH_3$ | $CH_3$ | 222– 3 |
| H | $SO_2N(CH_3)_2$ | H | n-$C_4H_9$ | 167– 9 |
| H | $SO_2N(CH_3)_2$ | H | n-$C_3H_7$ | 195– 7 |
| H | $SO_2N(CH_3)_2$ | H | $C_2H_5$ | 201– 3 |

EXAMPLE IV.

The following compounds are prepared from the appropriate $\beta$-keto ester



and benzofuroxan or a substituted benzofuroxan by adding the $\beta$-keto ester and then the benzofuroxan to a sodium ethoxide solution prepared from sodium pellets and ethanol, allowing the mixture to stand overnight and filtering, drying and recrystallising the precipitate from ethanol.



wherein:—

| X | Y | $R_7$ | $R_{16}$ |
|---|---|---|---|
| H | H | $C_2H_5$ | $CH_2OCOCH_3$* |
| Cl | H | $C_2H_5$ | $CH_2OCOCH_3$ |
| $CH_3$ | H | $C_2H_5$ | $CH_2OCOCH_3$* |
| $OCH_3$ | H | $C_2H_5$ | $CH_2OCOCH_3$ |
| $CF_3$ | H | $C_2H_5$ | $CH_2OCOCH_3$ |
| Cl | Cl | $C_2H_5$ | $CH_2OCOCH_3$ |
| H | H | $C_2H_5$ | $CH_2CN$*(a) |
| F | H | $C_2H_5$ | $CH_2CN$(a) |
| Cl | H | $C_2H_5$ | $CH_2CN$(a) |
| $CH_3$ | $CH_3$ | $C_2H_5$ | $CH_2CN$(a) |
| $SO_2NH_2$ | H | $C_2H_5$ | $CH_2CN$(a) |
| $OCH_3$ | H | $C_2H_5$ | $CH_2CN$(a) |
| H | H | $C_2H_5$ | $CH_2Cl$ |
| Cl | H | $C_2H_5$ | $CH_2Cl$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2Cl$ |
| H | H | $C_2H_5$ | $CH_2F$ |
| F | H | $C_2H_5$ | $CH_2F$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2F$ |
| $CF_3$ | H | $C_2H_5$ | $CH_2F$ |
| H | H | $C_2H_5$ | $CH_2SH$ |

TABLE (Continued)

| X | Y | $R_7$ | $R_{16}$ |
|---|---|---|---|
| Cl | H | $C_2H_5$ | $CH_2SH$ |
| F | H | $C_2H_5$ | $CH_2SH$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2SH$ |
| $CH_3$ | H | $C_2H_5$ | $CH_2SH$ |
| $CH_3$ | $CH_3$ | $C_2H_5$ | $CH_2SH$ |
| H | H | $CH_3$ | $CH(OCH_3)_2$ |
| Cl | H | $CH_3$ | $CH(OCH_3)_2$ |
| Cl | Cl | $CH_3$ | $CH(OCH_3)_2$ |
| H | H | $C_2H_5$ | $CH_2SCH_3$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2SCH_3$ |
| $OC_2H_5$ | H | $C_2H_5$ | $CH_2SCH_3$ |
| Cl | H | $C_2H_5$ | $CH_2SCH_3$ |
| $CH_3$ | $CH_3$ | $C_2H_5$ | $CH_2SCH_3$ |
| H | H | $C_2H_5$ | $CH_2NH_2$* |
| Cl | H | $C_2H_5$ | $CH_2NH_2$ |
| F | H | $C_2H_5$ | $CH_2NH_2$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2NH_2$ |
| $CF_3$ | H | $C_2H_5$ | $CH_2NH_2$ |
| $OCH_3$ | Cl | $C_2H_5$ | $CH_2NH_2$ |
| $CH_3$ | $CH_3$ | $C_2H_5$ | $CH_2NH_2$ |
| $SO_2NH_2$ | H | $C_2H_5$ | $CH_2NH_2$ |
| $SO_2N(CH_3)_2$ | H | $C_2H_5$ | $CH_2NH_2$ |
| $CF_3$ | H | $C_2H_5$ | $CH_2SH$ |
| $SO_2NH_2$ | H | $C_2H_5$ | $CH_2SH$ |
| $SO_2N(CH_3)_2$ | H | $C_2H_5$ | $CH_2SCH_3$ |
| H | H | $C_2H_5$ | $CH_2OCH_3$ |
| Cl | H | $C_2H_5$ | $CH_2OCH_3$ |
| F | H | $C_2H_5$ | $CH_2OCH_3$ |
| $SO_2N(CH_3)_2$ | H | $C_2H_5$ | $CH_2OCH_3$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2OCH_3$* |
| $CF_3$ | H | $C_2H_5$ | $CH_2OCH_3$ |

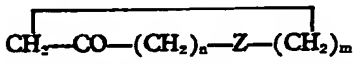
TABLE (Continued)

| X | Y | $R_7$ | $R_{16}$ |
|---|---|---|---|
| H | H | $C_2H_5$ | $CH_2OC_2H_5$ |
| Cl | H | $C_2H_5$ | $CH_2OC_2H_5$ |
| F | H | $C_2H_5$ | $CH_2OC_2H_5$ |
| $OCH_3$ | H | $C_2H_5$ | $CH_2OC_2H_5$ |
| H | H | $C_2H_5$ | $CH_2OC_6H_5$* |
| Cl | H | $C_2H_5$ | $CH_2OC_6H_5$ |
| $CF_3$ | H | $C_2H_5$ | $CH_2OC_6H_5$ |
| $OCH_3$ | Cl | $C_2H_5$ | $CH_2OC_6H_5$ |
| $SO_2NH_2$ | H | $C_2H_5$ | $CH_2OC_6H_5$ |
| H | H | $CH_3$ | $CH_2OCH_3$ |
| Cl | H | $CH_3$ | $CH_2OCH_3$ |
| $OCH_3$ | H | $CH_3$ | $CH_2OCH_3$ |

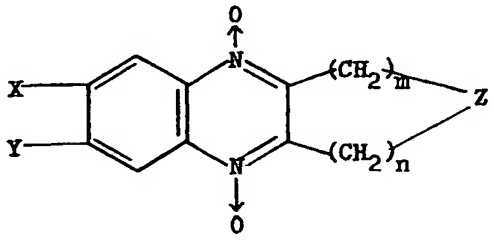
* Sodium hydride is used as base in these reactions in place of sodium ethoxide. (a) The corresponding 2-amino-3-carbethoxy compound is also formed.

## EXAMPLE V.

The following products are obtained by refluxing 0.01 moles of benzofuroxan with 0.1 moles of the appropriate heterocyclic ketone



in the presence of 8.7 g of morpholine and 50 mls. chloroform for 4 hours. The resulting mixture is then evaporated almost to dryness and filtered. The solid is recrystallised from acetone-hexane (1:1). The following products are obtained:—



plus the isomers thereof in those cases in which $m = n + 1$ wherein:—

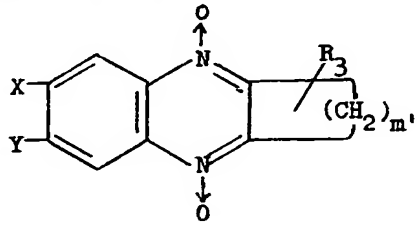
| X | Y | Z | m | n |
|---|---|---|---|---|
| H | H | NH | 0 | 2 |
| Cl | H | NH | 0 | 2 |
| F | H | NH | 0 | 2 |
| $OCH_3$ | H | NH | 0 | 2 |
| $CH_3$ | $CH_3$ | NH | 0 | 2 |
| $CF_3$ | H | NH | 0 | 2 |
| $SO_2NH_2$ | H | NH | 0 | 2 |
| $SO_2N(CH_3)_2$ | H | NH | 0 | 2 |
| H | H | $NCH_3$ | 0 | 2 |
| Cl | H | $NCH_3$ | 0 | 2 |
| $OCH_3$ | H | $NCH_3$ | 0 | 2 |
| Cl | Cl | $NCH_3$ | 0 | 2 |
| $CF_3$ | H | $NCH_3$ | 0 | 2 |
| $SO_2NH_2$ | H | $NCH_3$ | 0 | 2 |
| H | H | NH | 1 | 2 |
| Cl | H | NH | 1 | 2 |
| $OCH_3$ | H | NH | 1 | 2 |
| $CF_3$ | H | NH | 1 | 2 |
| $CH_3$ | $CH_3$ | NH | 1 | 2 |
| $SO_2NHCH_3$ | H | NH | 1 | 2 |
| H | H | $NCH_3$ | 1 | 2 |
| $CF_3$ | H | $NCH_3$ | 1 | 2 |
| Cl | H | $NCH_3$ | 1 | 2 |
| $OCH_3$ | Cl | $NCH_3$ | 1 | 2 |
| $SO_2N(CH_3)_2$ | H | $NCH_3$ | 1 | 2 |
| H | H | $NC_4H_9$ | 1 | 2 |
| Cl | H | $NC_4H_9$ | 1 | 2 |
| $OC_2H_5$ | H | $NC_4H_9$ | 1 | 2 |
| $CF_3$ | H | $NC_4H_9$ | 1 | 2 |
| H | H | $NC_6H_5$ | 1 | 2 |
| $OCH_3$ | Cl | $NC_6H_5$ | 1 | 2 |
| Cl | H | $NC_6H_5$ | 1 | 2 |
| Cl | H | $NC_7H_7$ | 1 | 2 |

TABLE (Continued)

| X | Y | Z | m | n |
|---|---|---|---|---|
| $CF_3$ | H | $NC_2H_5$ | 1 | 2 |
| H | H | NH | 1 | 3 |
| Cl | H | NH | 1 | 3 |
| $OCH_3$ | H | NH | 1 | 3 |
| $CH_3$ | H | NH | 1 | 3 |
| F | H | NH | 1 | 3 |
| $CF_3$ | H | NH | 1 | 3 |
| $SO_2NH_2$ | H | NH | 1 | 3 |
| $SO_2N(CH_3)_2$ | H | NH | 1 | 3 |
| H | H | O | 1 | 2 |
| Cl | H | O | 1 | 2 |
| F | H | O | 1 | 2 |
| $OCH_3$ | H | O | 1 | 2 |
| $CH_3$ | $CH_3$ | O | 1 | 2 |
| $CF_3$ | H | O | 1 | 2 |
| $SO_2NHCH_3$ | H | O | 1 | 2 |
| H | H | S | 1 | 2 |
| Cl | H | S | 1 | 2 |
| $OCH_3$ | H | S | 1 | 2 |
| $CF_3$ | H | S | 1 | 2 |
| F | H | S | 1 | 2 |
| $SO_2NH_2$ | H | S | 1 | 2 |
| $SO_2N(CH_3)_2$ | H | S | 1 | 2 |

## EXAMPLE VI.

The following 2,3-polymethylenequinoxaline-di-N-oxides are prepared by contacting 0.05 moles of benzofuroxan with 0.06 moles of an appropriate alicyclic ketone and 4.3 g morpholine in 300 ml benzene, refluxing the mixture for two hours allowing to cool and evaporating to dryness. The resulting product is triturated with an acetone-ether mixture (1:1), filtered and recrystallised.




wherein:—

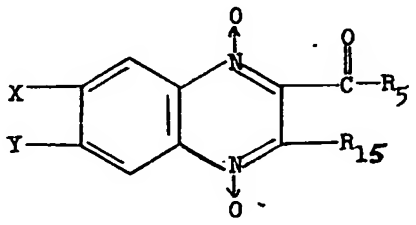
| 2,3-Polymethylene Moiety | X | Y |
|---|---|---|
| $-CH_2CH_2CH_2CH(COOH)-$ | H | H |
| $-CH_2CH_2CH(COOH)CH_2-$ | H | H |
| $-CH_2CH_2CH(COOH)CH_2-$ | Cl | H |
| $-CH_2CH(CH_3)CH(OH)-$ | H | H |
| $-CH_2CH_2CH(COOCH_3)-$ | H | H |
| $-CH_2CH_2CH(COOCH_3)-$ | $OCH_3$ | H |
| $-CH_2CH_2CH_2CH(OH)-$ | H | H |
| $-CH_2CH(COOCH_3)CH_2-$ | H | H |
| $-CH_2CH(NH_2)CH_2-$ | H | H |
| $-CH_2CH_2CH(NH_2)-$ | H | H |
| $-CH_2CH_2CH_2CH(COOH)-$ | F | H |
| $-CH_2CH_2CH_2CH(COOH)-$ | Cl | Cl |
| $-CH_2CH_2CH(COOH)CH_2-$ | $CH_3$ | H |
| $-CH_2CH(CH_3)CH(OH)-$ | Cl | H |
| $-CH_2CH(COOCH_3)CH_2-$ | $OCH_3$ | Cl |
| $-CH_2CH(NH_2)CH_2-$ | $OCH_3$ | H |
| $-CH_2CH(NH_2)CH_2-$ | Cl | H |
| $-CH_2CH(NH_2)CH_2-$ | $CF_3$ | H |
| $-CH_2CH(NH_2)CH_2-$ | $SO_2N(CH_3)_2$ | H |
| $-CH_2CH(COOCH_3)CH_2-$ | $CF_3$ | H |
| $-CH_2CH_2CH_2CH(OH)-$ | $CF_3$ | H |
| $-CH_2CH_2CH_2CH(OH)-$ | $SO_2NH_2$ | H |
| $-CH_2CH_2CH(Cl)-$ | H | H |
| $-CH_2CH_2CH(Cl)-$ | Cl | H |
| $-CH_2CH_2CH(Cl)-$ | $CF_3$ | H |
| $-CH_2CH_2CH(Cl)-$ | $OCH_3$ | H |
| $-CH_2CH_2CH(Cl)-$ | $SO_2NH_2$ | H |
| $-CH_2CH_2CH(Cl)-$ | $CH_3$ | $CH_3$ |
| $-CH_2CH_2CH(Br)-$ | H | H |
| $-CH_2CH_2CH_2CH(Cl)-$ | H | H |
| $-CH_2CH_2CH_2CH(Cl)-$ | Cl | H |
| $-CH_2CH_2CH_2CH(Cl)-$ | $OCH_3$ | Cl |

TABLE (Continued)

| 2,3-Polymethylene Moiety | X | Y |
|---|---|---|
| $-CH_2CH_2CH_2CH(Cl)-$ | $SO_2N(CH_3)_2$ | H |
| $-CH_2CH(CH_3)CH(OCH_3)-$ | H | H |
| $-CH_2CH(CH_3)CH(OCH_3)-$ | Cl | H |
| $-CH_2CH_2CH_2CH(OCH_3)-$ | H | H |
| $-CH_2CH_2CH_2CH(OCH_3)-$ | $OCH_3$ | H |
| $-CH_2CH_2CH_2CH(OCH_3)-$ | F | H |
| $-CH_2CH_2CH_2CH(OCH_3)-$ | $SO_2NHCH_3$ | H |
| $-CH_2CH_2CH(COCH_3)-$ | H | H |
| $-CH_2CH_2CH(COCH_3)-$ | Cl | H |
| $-CH_2CH_2CH(COCH_3)-$ | $OCH_3$ | H |
| $-CH(CH_3)CH_2CH_2CH(OH)-$ | H | H |
| $-CH(CH_3)CH_2CH_2CH(OH)-$ | $OCH_3$ | H |
| $-CH(CH_3)CH_2CH_2CH(OH)-$ | $OCH_3$ | Cl |
| $-CH(CH_3)CH_2CH_2CH(Cl)-$ | H | H |
| $-CH_2CH(CH_3)CH(OCOCH_3)-$ | H | H |
| $-CH_2CH(CH_3)CH(OCOCH_3)-$ | Cl | H |
| $-CH_2CH(CH_3)CH(OCOCH_3)-$ | $OCH_3$ | H |
| $-CH_2CH_2CH_2CH(OCOCH_3)-$ | H | H |
| $-CH_2CH_2CH_2CH(OCOCH_3)-$ | $CF_3$ | H |
| $-CH_2CH_2CH_2CH(OCOCH_3)-$ | $SO_2N(CH_3)_2$ | H |

## EXAMPLE VII.

Repetition of the procedure of Example I but using the appropriate $\beta$-diketone ($R_3COCH_2COR_4$) in place of acetylacetone and the appropriate benzofuroxan reactant produces the following compounds:



wherein:—

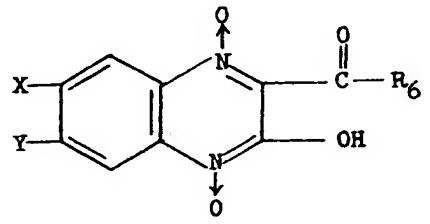
| $R_5$ | $R_{15}$ | X | Y |
|---|---|---|---|
| $C_6H_5$ | $CH_3$ | H | H |
| $C_6H_5$ | $CH_3$ | Cl | H |
| $C_6H_5$ | $CH_3$ | $OCH_3$ | H |
| $C_6H_5$ | $CH_3$ | F | H |
| $C_6H_5$ | $CH_3$ | $CF_3$ | H |
| $C_6H_5$ | $CH_3$ | $SO_2NHCH_3$ | H |
| $C_6H_5$ | $C_2H_5$ | H | H |
| $C_6H_5$ | i-$C_3H_7$ | H | H |
| $C(CH_3)_3$ | $C_6H_5$ | H | H |
| $CH(CH_3)_2$ | $C_6H_5$ | H | H |
| $CH_3$ | p-tolyl | H | H |
| $CH_3$ | p-tolyl | Cl | H |
| $CH_3$ | p-tolyl | $OCH_3$ | H |
| $CH_3$ | 4$(CH_3O)C_6H_4$ | H | H |
| $CH_3$ | 4$(CH_3O)C_6H_4$ | F | H |
| $CH_3$ | 4$(CH_3O)C_6H_4$ | $CF_3$ | H |
| $CH_3$ | 4$(CH_3O)C_6H_4$ | $SO_2NH_2$ | H |
| $CH_3$ | 4$(Br)C_6H_4$ | H | H |
| $CH_3$ | 4$(NO_2)C_6H_4$ | H | H |
| $CH_3$ | 4$(NO_2)C_6H_4$ | Cl | H |
| $C_6H_{13}$ | $C_6H_{13}$ | H | H |
| $C_6H_{13}$ | $C_6H_{13}$ | Cl | H |
| $C_6H_{13}$ | $C_6H_{13}$ | $CF_3$ | H |
| $C_6H_{13}$ | $C_6H_{13}$ | $OCH_3$ | Cl |
| $C_6H_{13}$ | $C_6H_{13}$ | $SO_2NHCH_3$ | H |
| $CH_3$ | $CH_3$ | $SO_2NH_2$ | H |
| $C_6H_5$ | $C_6H_5$ | Cl | H |
| $C_6H_5$ | $C_6H_5$ | F | H |
| $C_6H_5$ | $C_6H_5$ | $OCH_3$ | H |
| $C_6H_5$ | $C_6H_5$ | $SO_2N(CH_3)_2$ | H |
| $C_2H_5$ | $C_2H_5$ | Cl | H |

TABLE (Continued)

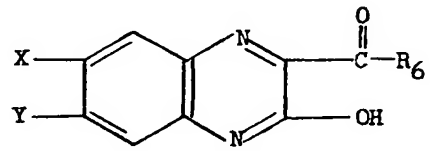
| $R_5$ | $R_{15}$ | X | Y |
|---|---|---|---|
| $C_2H_5$ | $C_2H_5$ | Cl | Cl |
| $C_2H_5$ | $C_2H_5$ | $SO_2NHCH_3$ | H |
| $C_2H_5$ | $C_2H_5$ | $CF_3$ | H |
| $C_2H_5$ | $C_2H_5$ | $OC_2H_5$ | H |

EXAMPLE VIII.

A mixture of 0.11 moles of an appropriate malonic acid diester is heated with 0.1 moles of benzofuroxan, 0.1 moles of sodium methoxide and 300 ml of methanol and allowed to stand overnight. The precipitate is filtered off, and the product isolated by acidification of the filtrate with 2N HCl followed by extraction with chloroform. Evaporation of the solvent yields the crude product, which is purified by crystallization from chloroform-hexane,



together with the reduced form:



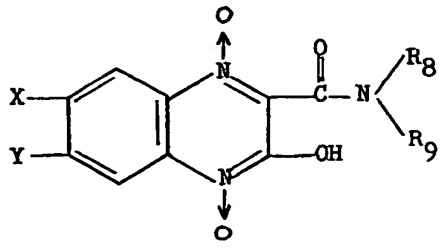
wherein:

| X | Y | $R_6$ |
|---|---|---|
| H | H | $OC_6H_5$ |
| Cl | H | $OC_6H_5$ |
| $OCH_3$ | H | $OC_6H_5$ |
| $CH_3$ | H | $OCH_3$ |
| $OC_2H_5$ | H | $OC_2H_5$ |
| $CF_3$ | H | $OC_6H_5$ |
| Cl | $OCH_3$ | $OCH_3$ |
| $CF_3$ | H | $OCH_3$ |
| $SO_2N(CH_3)_2$ | H | $OCH_3$ |
| $CH_3$ | $CH_3$ | n-$C_4H_9O$ |
| Cl | H | n-$C_4H_9O$ |
| F | H | n-$C_4H_9O$ |
| $SO_2NH_2$ | H | $OCH_3$ |
| $SO_2NH_2$ | H | n-$C_4H_9O$ |
| H | H | $OC_7H_7$* |
| Cl | H | $OC_7H_7$ |
| $OCH_3$ | H | $OC_7H_7$ |
| $SO_2NHCH_3$ | H | $OC_7H_7$ |

* Sodium hydride used as base in place of sodium methoxide.

## EXAMPLE IX.

The substitution of a malonamate that is a half-ester, half-amide of malonic acid for dimethylmalonate produces the following quinoxalines when reacted with the appropriate benzofuroxan according to the procedure of Example VIII.



wherein:—

| X | Y | $R_8$ | $R_9$ |
|---|---|---|---|
| H | H | H | H |
| Cl | H | H | H |
| F | H | H | H |
| $OCH_3$ | H | H | H |
| $CF_3$ | H | H | H |
| $CH_3$ | $CH_3$ | H | H |
| $SO_2N(CH_3)_2$ | H | H | H |
| Br | H | $CH_3$ | H |
| Cl | H | $CH_3$ | H |
| $OCH_3$ | H | $CH_3$ | H |
| $SO_2NH_2$ | H | $CH_3$ | H |
| H | H | $CH_3$ | $CH_3$ |
| $CF_3$ | H | $CH_3$ | $CH_3$ |
| Cl | H | $CH_3$ | $CH_3$ |
| $OCH_3$ | Cl | $CH_3$ | $CH_3$ |
| $SO_2NHCH_3$ | H | $CH_3$ | $CH_3$ |
| H | H | $C_2H_5$ | H |
| F | H | $C_2H_5$ | H |
| $OCH_3$ | H | $C_2H_5$ | H |
| $SO_2NH_2$ | H | $C_2H_5$ | H |
| H | H | i-$C_3H_7$ | H |
| H | H | n-$C_4H_9$ | H |
| Cl | H | n-$C_4H_9$ | H |
| H | H | $C_6H_5$ | H |
| Cl | H | $C_6H_5$ | H |
| $OCH_3$ | H | $C_6H_5$ | H |
| $SO_2N(CH_3)_2$ | H | $C_6H_5$ | H |
| H | H | $C_6H_5$ | $CH_3$ |
| Cl | H | $C_6H_5$ | $CH_3$ |
| H | H | $C_7H_7$ | H |
| $OCH_3$ | H | $C_7H_7$ | H |
| Br | H | $C_7H_7$ | $CH_3$ |

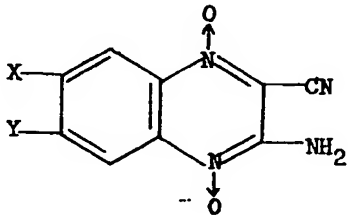
TABLE (Continued)

| X | Y | $R_8$ | $R_9$ |
|---|---|---|---|
| $CF_3$ | H | $C_6H_5$ | H |
| $SO_2NHCH_3$ | H | $C_6H_5$ | H |
| $OCH_3$ | Cl | $C_6H_5$ | H |
| Cl | Cl | $C_2H_5$ | $C_2H_5$ |
| $OC_2H_5$ | H | $CH_3$ | H |
| $CF_3$ | H | $C_2H_5$ | $C_2H_5$ |
| $CF_3$ | H | $C_3H_7$ | H |
| $SO_2NH_2$ | H | $C_3H_7$ | H |

The quinoxalines thus prepared are oxidized by known methods to the corresponding di-N-oxides. A favoured method comprises treating the quinoxaline in chloroform with an equimolar amount of m-chloroperbenzoic acid at room temperature for a period of three days. The precipitated m-chlorobenzoic acid is filtered off and the chloroform solution washed with saturated aqueous sodium bicarbonate. The chloroform solution is dried ($Na_2SO_4$) and taken to dryness under reduced pressure to give the product.

## EXAMPLE X.

0.3 moles of malonitrile are stirred with 0.25 moles of the appropriately-substituted benzofuroxan, 10 mls of triethylamine and 200 mls of tetrahydrofuran. After 30 minutes the reaction becomes violently exothermic and is controlled by an ice-bath. After reaction, the mixture is allowed to stand at room temperature for 24 hours. The resulting precipitate is filtered, dried and recrystallised from methanol. The following products are obtained:—

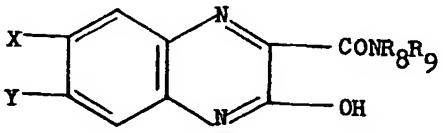


wherein:—

| X | Y |
|---|---|
| F | H |
| $SO_2NH_2$ | H |
| $SO_2N(CH_3)_2$ | H |
| $CF_3$ | H |
| $SO_2NHCH_3$ | H |

## EXAMPLE XI.

The following 3-hydroxy-2-quinoxalinecarboxamides are prepared from the appropriate malonic acid diamide (B—CO—$CH_2$—CO—B') and benzofuroxan by the procedure of Example X.



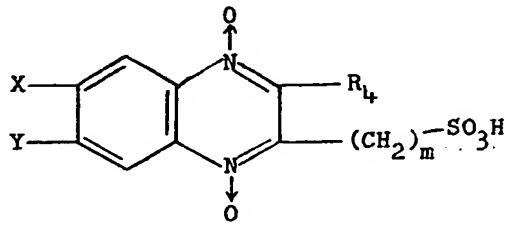
wherein:—

| X | Y | B | B' | $R_3$ | $R_9$ |
|---|---|---|---|---|---|
| H | H | $NH_2$ | $NH_2$ | H | H |
| Cl | H | $NH_2$ | $NH_2$ | H | H |
| H | H | $HNCH_3$ | $HNCH_3$ | H | $CH_3$ |
| Cl | H | $HNCH_3$ | $HNCH_3$ | H | $CH_3$ |
| $OCH_3$ | H | $HNCH_3$ | $HNCH_3$ | H | $CH_3$ |
| H | H | $HNC_6H_5$ | $HNC_6H_5$ | H | $C_6H_5$ |
| F | H | $HNC_6H_5$ | $HNC_6H_5$ | H | $C_6H_5$ |
| $CF_3$ | H | $HNC_6H_5$ | $HNC_6H_5$ | H | $C_6H_5$ |
| $SO_2NH_2$ | H | $HNC_6H_5$ | $HNC_6H_5$ | H | $C_6H_5$ |
| H | H | $NH_2$ | $HNC_6H_5$ | H | $C_6H_5$ |

Oxidation of these quinoxalines by the procedure set forth in Example X produces the corresponding di-N-oxides.

EXAMPLE XII.

The following compounds are prepared by stirring 0.1 moles of an appropriate benzofuroxan with 0.015 moles of ketosulfonic acid of the formula $R_4—CO—CH_2(CH_2)_m—SO_3H$, 0.025 moles of pyrrolidine and 20 mls of dimethylformamide at room temperature for 2—3 hours. The solid which separates is filtered off, washed with acetonitrile and dried.




wherein:—

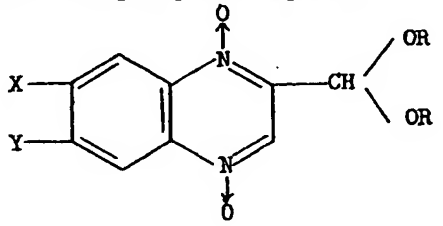
| X | Y | m—1 | $R_1$ |
|---|---|---|---|
| H | H | 0 | $CH_3$ |
| Cl | H | 0 | $CH_3$ |
| $OCH_3$ | H | 0 | $CH_3$ |
| $SO_2NH_2$ | H | 0 | $CH_3$ |
| H | H | 1 | $CH_3$ |
| Cl | H | 1 | $CH_3$ |
| F | H | 1 | $CH_3$ |
| $SO_3N(CH_3)_2$ | H | 1 | $CH_3$ |
| H | H | 1 | $C_6H_5$ |
| F | H | 1 | $C_6H_5$ |
| $OCH_3$ | H | 1 | $C_6H_5$ |
| $SO_2NHCH_3$ | H | 1 | $C_6H_5$ |
| $CF_3$ | H | 0 | $CH_3$ |
| $CF_3$ | H | 1 | $CH_3$ |

## EXAMPLE XIII.

### 2-Formylquinoxaline-di-N-Oxide Diacetals

Pyruvaldehyde dimethylacetal (26.0 g., 0.22 mole), benzofuroxan (27.2 g., 0.2 mole) and N,N-dimethylformamide (60 ml.) are placed in a three-necked round-bottomed flask and cooled to 0°—5°C. Ammonia (anhydrous) gas is passed through the stirred solution for thirty minutes at the end of which time the ammonia inlet tube is removed and replaced with a drying tube and the ammonia outlet tube replaced with a glass stopper. The reaction mixture is then allowed to stand at room temperature for five days. The product, 2-formyl-dimethylacetal-quinoxaline-di-N-oxide, is filtered off, slurried in ether, filtered and dried: M.P. 144—146.5°C., 72.3 percent yield.

In like manner the following compounds are prepared:

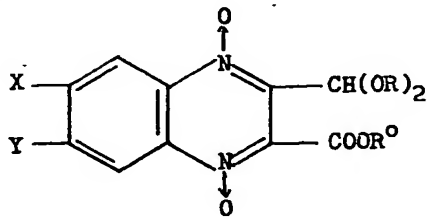



wherein:—

| X | Y | R | X | Y | R |
|---|---|---|---|---|---|
| H | H | $C_2H_5$ | $OCH_3$ | H | $CH_3$ |
| H | H | i-$C_3H_7$ | $SO_2NH_2$ | H | $CH_3$ |
| H | H | n-$C_4H_9$ | $CH_3$ | H | n-$C_4H_9$ |
| Cl | H | $CH_3$ | $SO_2N(CH_3)_2$ | H | n-$C_4H_9$ |
| F | H | $CH_3$ | Cl | H | n-$C_4H_9$ |
| $CH_3$ | Cl | $C_2H_5$ | $CF_3$ | H | $CH_3$ |

EXAMPLE XIV.

The following 2-carbalkoxy-3-formylquinoxaline-di-N-oxide diacetals are produced by stirring under nitrogen, 0.05 moles of a suitable alkyl γ,γ-dialkoxy aceto acetate and an appropriate benzofuroxan, and adding 50 mls of a 0.05 M solution of sodium ethoxide in ethanol. The mixture is stirred for three hours at room temperature and then refluxed for three more hours. After cooling to room temperature the mixture is stirred overnight, and concentrated to a viscous oil on a stream bath. Upon cooling, the oil solidifies. The solid is slurried with ethanol, and the purified solid filtered off. The product is recrystallised from hexane/acetone.




wherein:—

| X | Y | R | R° |
|---|---|---|---|
| Cl | H | $C_2H_5$ | $C_2H_5$ |
| F | H | $C_2H_5$ | $C_2H_5$ |
| $OCH_3$ | H | $C_2H_5$ | $C_2H_5$ |
| $CH_3$ | H | $C_2H_5$ | $C_2H_5$ |
| $CF_3$ | H | $C_2H_5$ | $C_2H_5$ |
| $SO_2NH_2$ | H | $C_2H_5$ | $C_2H_5$ |
| H | H | $CH_3$ | $C_2H_5$ |
| Cl | H | $CH_3$ | $C_2H_5$ |
| $OCH_3$ | H | $CH_3$ | $C_2H_5$ |
| H | H | $CH_3$ | $CH_3$ |
| H | H | n-$C_4H_9$ | n-$C_4H_9$ |
| Cl | H | n-$C_4H_9$ | n-$C_4H_9$ |
| $CH_3$ | H | n-$C_4H_9$ | n-$C_4H_9$ |
| H | H | n-$C_4H_9$ | $C_2H_5$ |
| $SO_2N(CH_3)_2$ | H | n-$C_4H_9$ | $C_2H_5$ |
| $SO_2NH(CH_3)$ | H | n-$C_4H_9$ | $C_2H_5$ |

The necessary alkyl γ,γ-dialkoxyacetoacetates are prepared according to the procedure described by Johnson and Cretcher, J. Am. Chem. Soc. *37* 2147—9 (1915) which comprises reacting the appropriate alkyldialkoxyacetate with sodium and an alkyl acetate. The procedure is exemplified below in the preparation of methyl γ,γ-dimethoxyacetoacetate.

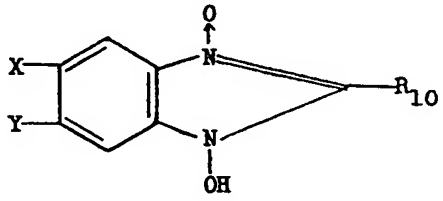
Sodium (56.2 g.) is dissolved in absolute ethanol (800 ml.) and the solution heated to 80°C. on a water bath. Dichloroacetic acid (105 g.) is then slowly added via a dropping funnel. The mixture is then cooled to 10°C., hydrochloric acid (35 ml.) in

absolute ethanol (50 ml.) is added and the solution allowed to stand at room temperature for eighteen hours. The hydrochloric acid is then neutralised by adding the stoichiometric amount of sodium ethylate in ethanol solution. The alcohol is removed by distillation under reduced pressure and the residue diluted by addition of cold water (20 ml.). The aqueous solution is extracted with ether (3 × 250 ml.), the ethereal solution dried and, after removal of the ether, distilled *in vacuo* to give ethyldiethoxyacetate.

Ethyldiethoxyacetate (32 g.) and methylacetate (25 g.) are placed in a flask equipped with stirrer and reflux condenser and heated to reflux. Metallic sodium wire (6.5 g.) is introduced into the flask in small portions and heating continued until the sodium is completely dissolved. Methylacetate (25 g.) and metallic sodium wire (6.5 g.) are then added and heating continued until the solution is clear. The mixture is cooled, a large volume of ice water cautiously added and the mixture extracted with ether. The aqueous solution is acidified with hydrochloric acid at 10°C. to 15°C. and the desired product extracted with ether. The ethereal extract is dried ($Na_2SO_4$), the ether removed and the residue distilled *in vacuo* to give methyl γ,γ-diethoxyacetoacetate.

## EXAMPLE XV.

The following compounds are prepared by adding dimethyl pyridine (11.3 g.), dropwise, to 0.12 moles of the appropriate primary nitro compound, 50 ml of tetrahydrofuran and 0.10 moles of the appropriate benzofuroxan. The reaction is controlled, if necessary, by an ice-bath to produce a steady reflux. On completion of the addition the resulting mixture is allowed to cool to room temperature, whereupon the solid product is filtered, washed with water, dried and recrystallised from a MeOH/$NaOCH_3$ mixture which is subsequently acidified.

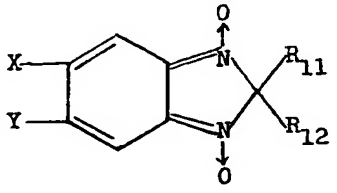



wherein:— Y=H and

| X | $R_{10}$ |
|---|---|
| Cl | H |
| F | H |
| $OCH_3$ | H |
| $CH_3$ | H |
| $CF_3$ | H |
| $SO_2NH_2$ | H |
| Cl | $CH_3$ |
| F | $CH_3$ |
| $OCH_3$ | $CH_3$ |
| $SO_2NHCH_3$ | $CH_3$ |
| Cl | $C_2H_5$ |
| $OCH_3$ | n-$C_3H_7$ |
| F | $CH_2CH_2CONH_2$ |
| $OCH_3$ | $CH_2CH_2CONH_2$ |
| $SO_2N(CH_3)_2$ | $CH_2CH_2CONH_2$ |
| $CF_3$ | $CH_2CH_2CONH_2$ |
| Cl | $COOC_2H_5$ |
| F | $COOC_2H_5$ |
| $OCH_3$ | $COOC_2H_5$ |

EXAMPLE XVI.

The following 2H-benzimidazole-1,3-di-N-oxides are prepared by adding dropwise 0.12 moles diethylamine to 0.10 moles of the appropriate benzofuroxan and 0.12 moles of the appropriate secondary nitro compound and allowing the reaction mixture to stand overnight at room temperature. The resulting solid is filtered, washed and dried.




wherein:— Y = H and:—

| X | $R_{11}$ | $R_{12}$ | X | $R_{11}$ | $R_{12}$ |
|---|---|---|---|---|---|
| Cl | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_2Br$ |
| F | $CH_3$ | $CH_3$ | F | $CH_3$ | $CH_2Br$ |
| $OCH_3$ | $CH_3$ | $CH_3$ | $OCH_3$ | $CH_3$ | $CH_2Br$ |
| $CF_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_2OH$ |
| $SO_2N(CH_3)_2$ | $CH_3$ | $CH_3$ | Cl | $CH_3$ | $CH_2OH$ |
| Cl | $CH_3$ | $C_2H_5$ | $OCH_3$ | $CH_3$ | $CH_2OH$ |
| $OCH_3$ | $CH_3$ | $C_2H_5$ | $SO_2N(CH_3)_2$ | $CH_3$ | $CH_2OH$ |
| $CH_3$ | $CH_3$ | $C_2H_5$ | H | $C_2H_5$ | $CH_2N(C_2H_5)_2$ |
| $SO_2NH_2$ | $CH_3$ | $C_2H_5$ | $OCH_3$ | $C_2H_5$ | $CH_2N(C_2H_5)_2$ |
| Cl | $-CH_2CH_2CH_2CH_2CH_2-$ | – | F | $C_2H_5$ | $CH_2N(C_2H_5)_2$ |
| $OCH_3$ | $-CH_2CH_2CH_2CH_2CH_2-$ | – | $SO_2NH_2$ | $C_2H_5$ | $CH_2N(C_2H_5)_2$ |
| F | $-CH_2CH_2CH_2CH_2CH_2-$ | – | | | |
| $SO_2NH_2$ | $-CH_2CH_2CH_2CH_2CH_2-$ | – | | | |
| H | $CH_3$ | $CH_2Cl$ | | | |
| Cl | $CH_3$ | $CH_2Cl$ | | | |
| $OCH_3$ | $CH_3$ | $CH_2Cl$ | | | |
| $CH_3$ | $CH_3$ | $CH_2Cl$ | | | |
| $SO_2NHCH_3$ | $CH_3$ | $CH_2Cl$ | | | |
| $CF_3$ | $CH_3$ | $CH_2Cl$ | | | |

WHAT WE CLAIM IS:—

1. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a malonic acid diester in the presence of an alkali metal hydroxide or an alkali metal hydride.

2. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a malonamate in the presence of an alkali metal hydroxide, an alkali metal alkoxide, or an alkali metal hydride.

3. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a malonic acid diamide in the presence of a base.

4. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a $\beta$-keto ester in the presence of ammonia, a primary or secondary amine, or an alkali metal hydride.

5. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a $\beta$-diketone in the presence of ammonia, a primary or secondary amine or an alkali metal hydride.

6. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a $\beta$-keto amide in the presence of a tertiary amine, an alkali metal hydroxide, an alkali metal alkoxide or an alkali metal hydride.

7. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a primary or a secondary nitro compound in the presence of an alkali metal hydroxide, an alkali metal alkoxide or an alkali metal hydride.

8. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with malononitrile or cyano acetamide in the presence of an alkali metal hydride.

9. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a pyruvaldehyde acetal (other than the dimethyl acetal) in the presence of ammonia or a primary, secondary or tertiary amine.

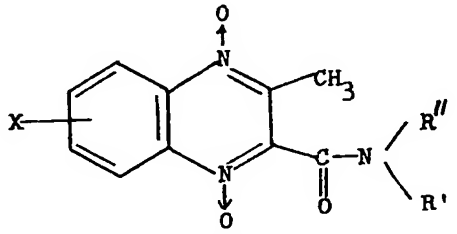
10. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with an alicyclic ketone in the presence of an alkali metal hydroxide, an alkali metal alkoxide or an alkali metal hydride.

11. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a heterocyclic ketone in the presence of ammonia, a primary, secondary or tertiary amine, an alkali metal hydroxide, an alkali metal alkoxide, or an alkali metal hydride.

12. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a ketosulfonyl compound or a ketosulfonamide in the presence of a base.

13. A process according to Claim 1 of British Patent No. 1,215,815 wherein an isobenzofuroxan is contacted with a lower alkyl, γ,γ-di(lower alkoxy) acetoacetate (other than the ethyl γ,γ-diethoxyacetoacetate) in the presence of ammonia, a primary, secondary or tertiary amine, an alkali metal hydroxide, an alkali metal alkoxide or an alkali metal hydride.

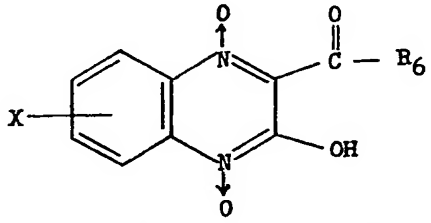
14. A compound of the formula



wherein X is fluoro, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituted positions of the benzene nucleus, the substituent in each position being the same or different; and each of R′ or R″ is hydrogen or lower alkyl.

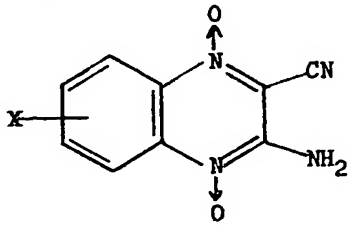
15. 3-Methyl-6 (or 7)-fluoro-2-quinoxalinecarboxamide-di-N-oxide.

16. A compound of the formula



wherein $R_6$ is lower alkoxy, aryloxy, benzyloxy or $NR_7R_8$ wherein $R_7$ and $R_8$ are hydrogen, lower alkyl or phenyl; and X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different, the compounds 2-carbomethoxy-3-hydroxy quinoxaline-di-N-oxide and 2-carboethoxy-3-hydroxyquinoline-di-N-oxide being excluded.

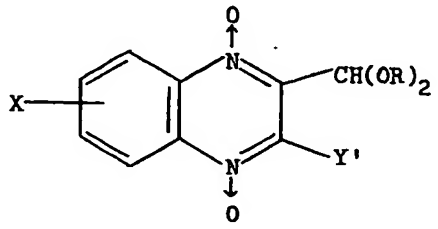
17. A compound of the formula



wherein X is fluoro, trifluoromethyl, sulfonamido, N-methylsulfonamido or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different.

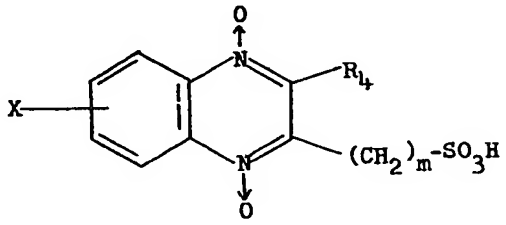
18. 2-Cyano-3-amino-6 (or 7)-fluoroquinoxaline-di-N-oxide.

19. A compound of the formula



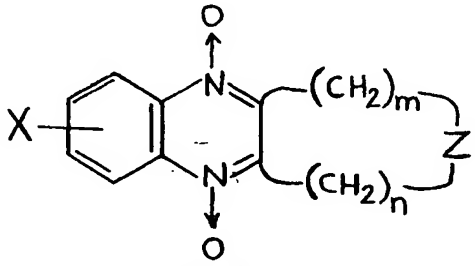
wherein R is lower alkyl; X is hydrogen, chloro, fluoro, methyl, methoxy, trifluoromethyl, sulfonamido, N-methylsulfonamido, or N,N-dimethylsulfonamido and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; and Y' is hydrogen or carbo-(lower alkoxy), the compounds 2-formyl-dimethyl-acetal quinoxaline di-N-oxide and 2-carboethoxy-3-formyl-di-ethyl acetal-quinoxaline di-N-oxide being excluded.

20. A compound of the formula



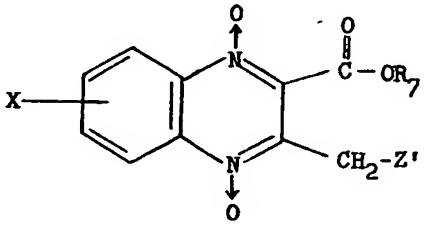
wherein X is as defined in Claim 19, $R_4$ is lower alkyl or phenyl; and m is 0 or 1.

21. A compound of the formula



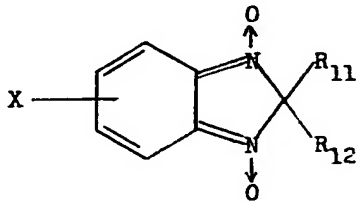
wherein X is as defined in Claim 19; Z is oxygen, sulphur, imino or N-methylimino, m is 0 or 1 and n is 2 or 3.

22. A compound of the formula



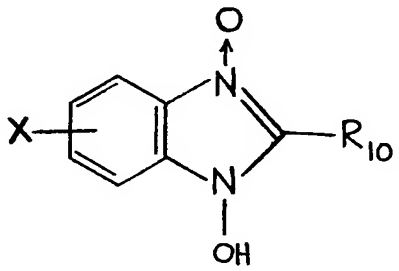
wherein X is as defined in Claim 19; $R_7$ is lower alkyl; and Z' is halogen, lower alkoxy, lower alkanoyloxy, cyano, phenoxy, amino, mercapto or lower alkylmercapto.

23. A compound of the formula



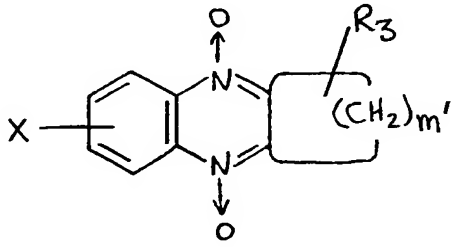
wherein X is hydrogen, methyl, fluoro, chloro, methoxy, sulfonamido, N-methyl-sulfonamido, N,N-dimethyl sulfonamido or trifluoromethyl and may be substituted in one or more of the four substituent positions of the benzene nucleus, the substituent in each position being the same or different; $R_{11}$ and $R_{12}$ are methyl, ethyl, a methyl or ethyl group substituted by a chloro, bromo, hydroxy or di-ethylamino group, or, when taken together with the carbon atom to which they are attached, are cyclohexyl, the compounds 2,2-dimethyl-2H-benzimidazole-1,3-dioxide and 2-methyl-2-ethyl-2H-benzimidazole-1,3-dioxide being excluded.

24. A compound of the formula



in which X is as defined in Claim 19, $R_{10}$ is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, carbalkoxy or carboxamido, the compounds 1-hydroxy-2-benzimidazole propionamide-3-oxide, and 1-hydroxy-2-carboethoxybenzimidazole-3-oxide being excluded.

25. A compound of the formula



in which X is as defined in Claim 19, m' is an integer of from 2 to 16, and $R_3$ is halogen, hydroxyl, alkoxy, acetoxy, alkyl, aryl, acetyl, amino, alkylamino, arylamino, acylamino, aroylamino, carboxy, carbalkoxy, nitrile or amido.

26. Compounds when prepared in accordance with any one of Claims 1 to 13 and substantially as hereinbefore described with reference to the Examples.

27. Methods of preparing quinoxaline di-N-oxides, benzimidazole-di-N-oxides, and 1-hydroxy-benzimidazole-3-oxides according to any one of Claims 1 to 13 and substantially as hereinbefore described with reference to the Examples.

28. Compounds in accordance with any one of Claims 14 to 25 substantially as hereinbefore described in any one of the Examples.

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